

## **REMARKS**

The amendments to the claims find support in the specification and claims as originally filed. For example, the amendments to Claims 1 and 5 find support in the specification as filed at pages 12-13 (e.g., page 12, lines 19-20) and elsewhere in the specification. The amendment to Claim 8 deletes words, and the amendment to Claim 21 finds support in the specification, for example, at page 7, lines 6-7, and elsewhere in the specification. No new matter is added by the amendments.

Applicant acknowledges the grant of the petition to accept the priority claim under 35 U.S.C. §119(e) and the acceptance of the drawings filed on December 19, 2001.

Claims 1-24 are pending in the application. Claims 1-21 stand rejected, and Claims 22-24 stand withdrawn from consideration.

Claims 1-3, 5-7, and 9-11 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 8 and 21 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. (The Examiner's discussion of this rejection being directed to Claim 21, Applicant believes that Claim 21 was meant when the numeral "12" was typed on page 3, line 5 of the Office Action.)

Claims 1, 3, 5, 7, 9-14, 16, 17 and 19-21 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by McGall et al. (U.S. Patent 5,412,087, hereafter "McGall").

Claims 1, 4, 5, and 8 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Wybourne et al. (U.S. Patent No. 5,465,151, hereafter "Wybourne").

Claims 2, 6, 15, and 18 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious over McGall in view of Eggers et al. (U.S. Patent No. 5,532,128, hereafter "Eggers").

Applicant respectfully traverses the rejections of Claims 1-21 and the withdrawal of Claims 22-24.

**The Rejections of Claims 1-3, 5-7 and 9-11 Under 35 U.S.C. §112, First Paragraph**

Claims 1-3, 5-7, and 9-11 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, the Examiner alleging that the specification and claims as originally filed do not "give proper support for a heterobifunctional spacer comprising a genus of biotinamide." Applicant acknowledges the Examiner's statement that the specification "supports the species of heterobifunctional spacer comprising succinimidyl-6-(biotinamido)hexanoate."

Although not acquiescing to this characterization of the claims and of the specification, and explicitly reserving the right to pursue claims directed to compositions and methods comprising a heterobifunctional spacer comprising a genus of biotinamide, in order to expedite the allowance of the application, applicants have amended Claims 1 and 5 to recite a heterobifunctional spacer comprising succinimidyl-6-(biotinamido)hexanoate.

Accordingly, Applicant respectfully submits that the rejections of Claims 1-3, 5-7, and 9-11 under 35 U.S.C. §112, first paragraph, are overcome.

**The Rejections of Claims 8 and 21 Under 35 U.S.C. §112, Second Paragraph**

Claims 8 and 21 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiner alleges that Claim 8 is grammatically unclear for reciting the phrase "wherein the soft base heterobifunctional spacer is"; the Examiner also alleges that the limitation "said oligonucleotide" in Claim 21 lacks sufficient antecedent basis. In order to expedite prosecution of the claims to allowance, and without acquiescence to the grounds for these rejections, applicants have amended Claims 8 and 21.

Applicant respectfully submits that amended Claims 8 and 21 are not indefinite. Accordingly, Applicant respectfully submits that the rejections of Claims 8 and 21 under 35 U.S.C. §112, second paragraph, are overcome.

**The Rejections of Claims 1, 3, 5, 7, 9-14, 16, 17, and 19-21 Under 35 U.S.C. §102(b)**

Claims 1, 3, 5, 7, 9-14, 16, 17, and 19-21 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by McGall (U.S. Patent No. 5,412,087). However, anticipation under 35 U.S.C. §102 requires that “every element of the claimed invention be identically shown in a single reference.” (*In re Bond*, 910 F.2d 831,832 (Fed. Cir. 1990). Applicant respectfully submits that McGall fails to disclose every element of the claimed invention, and thus fails to anticipate Claims 1, 3, 5, 7, 9-14, 16, 17, and 19-21.

McGall clearly states that the coupling of the oligonucleotides discussed in McGall's Example 3, cited by the Examiner, is a covalent attachment (column 14, lines 65-68) to a glass substrate: “This example shows the results of a test for the effectiveness of several different thiol-reactive groups that, when attached to an oligonucleotide, enable covalent coupling to thiol-derivatized glass slides.”

The inventions of Claims 1, 3, 5, 7, 9-14, 16, 17, and 19-21 require, among other elements, a soft metal solid support and a heterobifunctional spacer chemi- or physisorbed to said soft metal solid support via soft metal-soft base bonding. However, McGall discusses attachment to glass substrates, not a soft metal solid support as required by the present invention; and McGall discusses covalent attachment, not the attachment required by the present claims, in which the heterobifunctional spacer must be “chemi- or physisorbed to said soft metal solid support via soft metal-soft base bonding.” Moreover, McGall claims that haloacetyl activating groups do not work, stating at column 15, lines 45-49 that “[t]he results show that none of the haloacetyl activating groups enhanced binding significantly above the background non-specific binding ...”. McGall nowhere discusses soft-metal soft base bonding, nor a spacer being chemi- or physisorbed to said soft metal solid support via soft metal-soft base

bonding, nor a heterobifunctional spacer being chemi- or physisorbed to said soft metal solid support via soft metal-soft base bonding.

Thus, McGall fails to disclose elements of Claims 1, 3, 5, 7, 9-14, 16, 17, and 19-21 including attachment of a heterobifunctional spacer to a soft metal solid support; chemi- or physisorption of a heterobifunctional spacer to a soft metal solid support; and soft metal-soft base bonding of a heterobifunctional spacer to a soft metal solid support. For at least these reasons, McGall fails to anticipate Claims 1, 3, 5, 7, 9-14, 16, 17, and 19-21.

Accordingly, in the absence of any direct or indirect disclosure regarding these and other elements, Applicant respectfully submits that Claims 1, 3, 5, 7, 9-14, 16, 17, and 19-21 are not anticipated by McGall.

#### **The Rejections of Claims 1, 4, 5, and 8 Under 35 U.S.C. §102(b)**

Claims 1, 4, 5, and 8 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Wybourne (U.S. Patent No. 5,465,151). Applicant respectfully submits that Wybourne fails to disclose every element of the claimed invention, and thus fails to anticipate Claims 1, 4, 5, and 8.

Wybourne discusses covalent attachment of molecules to a polystyrene substrate. For example, the Examiner cites Wynbourne column 28, lines 13-14 as discussing succinimidyl-6-(biotinamido)hexanoate. However, the compound succinimidyl-6-(biotinamido)hexanoate is discussed by Wybourne merely as an intermediate in the synthesis of N-4-azido-2,3,5,6-tetrafluorobenzyl-6-(biotinamido)hexanimide (see column 28, lines 11-16). Wynbourne does not discuss the use of succinimidyl-6-(biotinamido)hexanoate as a heterobifunctional spacer.

Moreover, the Example cited by the Examiner does not discuss attachment of a molecule to a soft metal substrate; instead, it is directed to the functionalization of "a polymer surface" (column 26, lines 63-64). In addition, Wybourne fails to discuss a spacer that is chemi- or physisorbed to a soft metal solid support. Thus, Wybourne fails to discuss non-covalent, soft metal-soft base bonding to a soft metal substrate as

required by the claims. In addition, Wybourne never discusses succinimidyl-6-(biotinamido)hexanoate as a heterobifunctional spacer, and never discusses succinimidyl-6-(biotinamido)hexanoate as a heterobifunctional spacer that may be non-covalently bound to a soft metal substrate via soft metal-soft base bonding. Accordingly, Wybourne lacking at least these elements of the claimed invention, Applicant respectfully submits that Claims 1, 4, 5, and 8 are not anticipated by Wybourne.

#### **The Rejections of Claims 2, 6, 15, and 18 Under 35 U.S.C. §103(a)**

Claims 2, 6, 15, and 18 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious over McGall in view of Eggers (U.S. Patent No. 5,532,128).

In order to establish a prima facie case of obviousness, there must be 1) some suggestion or motivation in the art or in the knowledge generally available to one of ordinary skill in the art, to modify or to combine the reference teachings; 2) there must be a reasonable expectation of success; and 3) the prior art references must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, and not based on the applicant's disclosure. In re Vaack, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

However, as discussed above, McGall clearly states that the coupling of the oligonucleotides discussed in McGall's Example 3, cited by the Examiner, is a covalent attachment (column 14, lines 65-68) to a glass substrate. McGall fails to discuss non-covalent immobilization of oligonucleotides on a metal substrate involving the use of heterobifunctional reagents such as succinimidyl 6-[6-((iodoacetyl)amino)hexanoyl]amino)hexanoate]. The present claims are directed to non-covalent attachment of heterobifunctional spacers to a soft metal solid support.

McGall is further cited by the Examiner as discussing "[h]ybridization of the produce array to the target nucleic acid" referring to column 16, lines 25-46. However,

column 16, lines 25-46 of McGall is directed to glass slides (column 16, line 25) and not to a soft metal solid support as required by the present claims.

The Examiner also discusses crosslinking groups and crosslinking reagents, citing the discussion of McGall at column 6, lines 43-47 and 50-64. However, in this discussion, McGall states "provided only that caged thiols can be attached to the surface of the substrate. Preferably, the surface will contain reactive groups...." (column 6, lines 32-34). Applicant notes that McGall nowhere discusses soft-metal soft base bonding, nor a spacer being chemi- or physisorbed to said soft metal solid support via soft metal-soft base bonding, which are elements required by the present claims.

The Examiner notes that the McGall does not "explicitly teach that the metal is selected from the list of metals recited in instant Claims 2, 6, 15, and 18."

Eggers is cited by the Examiner to provide the "concept of linking a thiol group to a metal substrate such as gold, platinum, titanium, etc. (column 8, lines 30-35) to create an array of probes."

However, Eggers nowhere discusses a spacer that is "chemi- or physisorbed to said soft metal solid support via soft metal-soft base bonding" as required by the instant claims. Moreover, Eggers fails to discuss a ligand-binding solid surface comprising a soft metal solid support and a spacer that is "chemi- or physisorbed to said soft metal solid support via soft metal-soft base bonding." Eggers also fails to discuss any method for preparing such a ligand-binding solid surface and fails to discuss methods utilizing such a ligand-binding solid surface.

Eggers nowhere discusses a haloacetyl or an iodoacetyl group. Eggers, as well as McGall, fail to discuss succinimidyl-6-(biotinamido)hexanoate as a soft base suitable for use in a spacer that may be chemi- or physisorbed to a soft metal support via soft metal-soft base bonding.

The instant claims require a soft base chemi- or physisorbed to a soft metal solid support via soft metal-soft base bonding, which is nowhere is discussed in the cited references. In addition, since McGall claims that haloacetyl activating groups do not work (e.g., column 15, lines 45-49), and so teaches away from elements of the present

invention, one would have no motivation to combine the discussion of McGall related to such groups with any other reference, and one would have no reasonable expectation of success even if the cited references were to be combined. Thus, the cited references also fail to provide motivation to combine with other references to provide the claimed invention, and fail to provide a reasonable expectation of success even if the cited references were to be combined.

For at least these reasons, the combination of McGall in view of Eggers fails to disclose all the elements of Claims 2, 6, 15, and 18; fail to provide motivation to combine these references to provide the claimed invention; and fail to provide reasonable expectation of success were the references to be so combined.

Accordingly, Applicant respectfully submits that Claims 2, 6, 15, and 18 are not made obvious by the cited references.

#### **The Requirement to Cancel Claims 22-24 as Directed to a Non-elected Invention**

Claims 22-24 stand withdrawn as allegedly directed to a non-elected invention. The Examiner suggests that Claims 22-24 "are drawn to a patentably distinct method of recovering a ligand via use of steps and elements which are not useable together as the previously examined methods." Applicant respectfully submits that Claims 22-24 are drawn to methods that are indeed useable together with the previously examined methods.

Applicant respectfully draws the Examiner's attention to Claims 1 and 5, which include "a heterobifunctional spacer ... including a soft base" where the soft base may be, or may include, iodine. Independent Claims 1, 5, 14 and 17, and claims dependent thereon or referring thereto, are directed to heterobifunctional spacers and their use. As indicated above, such heterobifunctional spacers may include iodine or iodine-containing groups. Thus, even though the previously examined claims did not explicitly recite "thiodiglycol," Claims 22-24 are directed to methods for use with the subject matter of Claims 1-21.

The use of thiodyglycol, an element of Claims 22-24, is disclosed in the specification at, for example, pages 15-16 and is clearly usable with the previously examined methods. For example, the discussion in Example 4 with regard to the methods claimed in Claims 22-24 explicitly refers (page 16, line 5) to the method of Example 3, in which a succinimidyl-6-[6-(((iodoacetyl)amino)-hexanoyl-amino] hexanoate) spacer is discussed (page 14, lines 24-26). Such a spacer, containing an iodoacetyl group, clearly falls within the subject matter of Claims 1 and 5 and their dependent claims, and so is the subject matter of the previously examined methods. Methods for the recovery of ligands immobilized by the heterobifunctional spacers of the previously examined claims are related to those, and the other, previously examined independent and dependent claims, and such methods are clearly usable together with the previously examined claims.

Accordingly, for at least these reasons, Applicant submits that the subject matter of Claims 22-24 is related to, and usable with, the previously examined claims. Applicant respectfully requests that Claims 22-24 be examined with the present claims. Applicant notes that Claims 22-24 are directed to methods related to the claimed heterobifunctional spacers chemi- or physisorbed on a silver-containing support via soft metal-soft base binding, and further note that no reference discloses such heterobifunctional spacers, nor ligand-binding solid surfaces comprising such heterobifunctional spacers, nor methods for recovering ligands from such heterobifunctional spacers. Accordingly, Applicant submits that Claims 22-24 are allowable over the art and request their allowance.

### **CONCLUSION**

Applicant respectfully submits that Claims 1-24 stand in allowable form, and respectfully request their examination and allowance of all claims, including Claims 22-24. Early notification of the allowance of the application is respectfully requested.



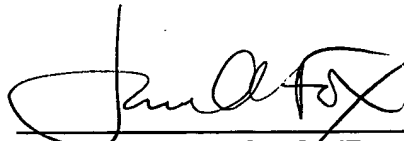
The Examiner is invited to contact the undersigned attorney at the telephone number indicated below should he find that there are any further issues outstanding.

Please charge any fees, including fees for extension of time, or credit overpayment to Deposit Account No. 08-1641, referencing Attorney's Docket No. 25527-0001 C1.

Respectfully submitted,

Dated: September 2, 2004

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